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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/459,062	12/10/1999	TAO TAO	17634-00034U	9639

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NATIONAL INSTITUTES OF HEALTH
OFFICE OF TECHNOLOGY TRANSFER
6011 EXECUTIVE BLVD SUITE 325
ROCKVILLE, MD 20852-3804

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/459,062	TAO ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *31-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30 and 46-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *04 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response to the Office action of November 15, 2005, filed February 15, 2006, is acknowledged. No claim amendments were made. Claims 1-74 are pending. Claims 31-45 remain withdrawn from consideration, being drawn to non-elected subject matter. Claims 56 and 57 are rejoined with the elected invention. Claims 1-30 and 46-74 are under examination. (Note that claim 13 lacks a period at the end of the sentence.)

Claim Rejections - 35 USC § 112

2. The rejection of claims 11, 13 and 16-18 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that rPIV3-2TM, rPIV3-2TM*cp*45, rPIV3-2CT and rPIV3-2CT*cp*45 are required to practice the claimed invention because they are a necessary limitation for the success of the invention as stated in the claims. As a required element they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the viral constructs. See 37 CFR 1.802. One cannot practice the claimed invention without access to those particular viruses. The specification does not provide a repeatable method for obtaining exactly those constructs without access to rPIV3-2TM, rPIV3-2TM*cp*45, rPIV3-2CT and rPIV3-

2CT*cp*45 and they do not appear to be readily available material. Deposit of rPIV3-2TM, rPIV3-2TM*cp*45, rPIV3-2CT and rPIV3-2CT*cp*45 in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112, because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the constructs rPIV3-2TM and rPIV3-CT are derived from the genomes of HPIV2 and HPIV3, see Example 6 and Figures 7-8. Applicant asserts that HPIV2 and HPIV3 viruses are available from the ATCC (VR-92 and VR-93, respectively). Applicant argues that cloning the genomes of these viruses into a form recoverable from cDNA was described in Applicant's prior publications and papers (Durbin *et al.,* 1996). Applicant also asserts that rPIV3-2TM can be described as containing regions from the transmembrane domains of HN and F genes from HPIV2 and HPIV3 background. In the same way, rPIV3-CT construct contains coding regions from both the transmembrane domains and ectodomains of HN and F HPIV2 genes in an HPIV3 background. Applicant points to Figure 9, SEQ ID NO: 40 and 41, for the cDNAs bearing the rPIV3-2TM and rPIV3-CT construct. Applicant asserts that 12 cp45 mutations were introduced into the PIV3 portions of the rPIV3-TM and rPIV3-CT constructs to obtain the derivatives rPIV3-2TMcp45 and rPIV3-2CTcp45.

In response to Applicant's arguments, the question of enablement in this case is directed to access to a specific virus(es) that has a laboratory designation. While one of skill in the art would be able to make similar construct, the exact construct of rPIV3-TM and rPIV3-CT is not attainable without being deposited. If Applicant intends to claim the construct in general terms, and not by laboratory designation, the construct may be explained in words rather than by a

specific name, as in other claims of the instant application. As for SEQ ID NO: 40 and 41, the cDNAs of the antigenomes of the rPIV3-2TM and rPIV3-CT construct are not sufficient to provide access to the actual rPIV3-2TM and rPIV3-CT constructs. In other words, claiming a specific laboratory designated virus requires access to that virus. Claiming a virus that has the same structural organization as the specific virus is acceptable because one of skill in the art is capable of making a similar virus without access to the laboratory designated virus. Therefore, the rejection is maintained for reasons of record because the invention requires access to the exact viruses of rPIV3-2TM, rPIV3-2TM*cp*45, rPIV3-2CT and rPIV3-2CT*cp*45.

3. Claims 26 and 71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are drawn to chimeric viruses, specifically wherein the substitution mutation at position 456 of the L protein is "to another amino acid". The breadth of the claims has not been adequately described such that one of skill in the art would know how to practice the invention.

The specification describes a mutation wherein the amino acid at position 456 of PIV3 is changed to leucine. However, Applicant's claims encompass a substitution of any of the 20 amino acids. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical

and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is one example (456 F) out of 20 possibilities and no particular function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Applicant's arguments have been carefully considered but fail to persuade. Applicant argues that the Federal Circuit states that a sequence need not appear in a patent specification to support a DNA-based invention provided that the state of the scientific knowledge at the time the application was filed includes such structural information. Applicant cites *Capon et al. v. Eshhar et al. v. Dudas*, 76 USPQ2d 1098 (Fed. Cir. 2005). [Note that the citation is 76 USPQ2d 1078, not 1098.] Applicant argues that the skilled artisan would be fully aware of the structure of the genus of polypeptides claimed. Applicant asserts that the skilled artisan would merely have to replace the nucleotide sequence encoding an amino acid at the specific location recited in the claims with any of the well-known nucleotide sequences that encode the desired amino acid.

In response to Applicant's arguments, the examiner has considered *Capon et al. v. Eshhar et al. v. Dudas*, 76 USPQ2d 1078 (Fed. Cir. 2005). Capon *et al.* and Eshhar *et al.* disclosed the sequences of those that were to be recombined. The Fed Circuit noted in section [1], that "since written description requirement must be applied in context of particular invention and state of knowledge, and there is no per se rule that nucleotide sequence must be recited anew when that information is already known in art, since invention at issue lies not in discovering which DNA segments are related to immune response, but in novel combination of segments to

achieve novel result, since claimed chimeric genes are prepared from known DNA sequence of known function, and since requirement that these sequences be analyzed and reported in specifications therefore does not add descriptive substance."

In this case, Applicant has provided a base structure in which the nucleotides encoding an amino acid are to be substituted for the naturally occurring nucleotides encoding a different amino acid. In *Capon et al. v. Eshhar et al. v. Dudas*, the sequences to be combined were provided in full. Applicant has provided the nucleotides to be substituted into the base structure, and points to the known nucleotides that are available which encode amino acids. The Office assumes that Applicant is referring to at least the 60 codons that encode the 20 common amino acids: gca, gcc, gcg, gcu, ugc, ugu, gac, gau, gaa, gag, uuc, uuu, gga, ggc, ggg, ggu, cac, cau, aua, auc, auu, aaa, aag, uua, uug, cua, cuc, cug, cuu, aug, aac, aau, cca, ccc, ccg, ccu, caa, cag, aga, agg, cga, cgc, cgg, cgu, agc, agu, uca, ucc, ucg, ucu, aca, acc, acg, acu, gua, guc, gug, guu, ugg, uac and uau.

While the sequences are provided in full, as in *Capon et al. v. Eshhar et al. v. Dudas,* the function of the substituted codon is not known. In *Capon et al. v. Eshhar et al. v. Dudas*, the invention of Capon does not concern the discovery of gene function or structure, but are prepared from known DNA sequences of known function. On this point, *Capon et al. v. Eshhar et al. v. Dudas*, and the instant application differ.

In this case, the function of the codons in the base structure is not known. Applicant has failed to provide a structure/function nexus between the substituted codon (structure) and its desired function (attenuation). For Applicant to claim a genus of substitutions for which Applicant has not given a starting point, one of skill in the art would need to discover which of

gca, gcc, gcg, gcu, ugc, ugu, gac, gau, gaa, gag, uuc, uuu, gga, ggc, ggg, ggu, cac, cau, aua, auc, auu, aaa, aag, uua, uug, cua, cuc, cug, cuu, aug, aac, aau, cca, ccc, ccg, ccu, caa, cag, aga, agg, cga, cgc, cgg, cgu, agc, agu, uca, ucc, ucg, ucu, aca, acc, acg, acu, gua, guc, gug, guu, ugg, uac and uau, is an attenuating mutation. In other words, if Applicant had provided a nexus, such as hydrophilic amino acids can be substituted for position 456 of the L protein, one of skill in the are would be have a connection between the substitution and the function of attenuation. Applicant has not provided this. Therefore, the claims remain rejected for reasons of record.

Claim Rejections - 35 USC § 102

4. Claims 1-10, 12, 19-23, 25, 28-30, 46-49, 53-59, 65, 66 and 77-74 remain rejected under 35 U.S.C. 102(e) as being anticipated by Belshe *et al.* (US 5,869,036, "Belshe"). The summary of claims and teachings of Belshe are of record. With regard to the new claims, their subject matter is directed to the same subject matter previously claimed.

The claims are directed to infectious chimeric PIVs having a human PIV background genome and a chimeric glycoprotein from another antigenically distinct HPIV. Belshe teaches hybrid viruses having glycoproteins exchanged between HPIV1, HPIV2 and HPIV3 (as a background genome), see abstract and Example 7).

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

Applicant argues that Belshe discloses the cp45 genome in schematic form and provides a summary description of hybrids thereof. Applicant asserts that the hybrid genomes are derived by replacing the regions encoding the cp45 glycoproteins with cDNA copies of corresponding

gene of a "target" virus (col. 9, lines 54-59 and col. 10, lines 19-22). Applicant asserts that Belshe replaces the entire gene, rather than a structural domain, antigenic domain or epitope of the gene. Applicant argues that Belshe's disclosure of entire gene replacement does not read on the instant claims which are drawn to a "chimeric glycoprotein", which is not a complete replacement of the background gene.

In response to Applicant's arguments, the Office recognizes that Applicant is attempting to argue that the recited "chimeric glycoprotein" means that a portion of the background gene and a portion of the heterologous gene are both present in the encoded chimeric glycoprotein. The claims now indicate that a structural domain, antigenic domain or epitope of the heterologous gene (or encoded protein) is incorporated into the background genome, but that neither the background gene or the heterologous gene is completely present in the chimeric gene.

Applicant is attempting to limit the meaning of "incorporate" to exclude complete gene replacement. Belshe's description of replacing background glycoproteins with cp45 glycoproteins is encompassed by the instant claim language. If one were to replace the entire HN ectodomain (surface protein) from PIV3 with cp45 HN ectodomain, the remaining portions of the non-ectodomain protein are expected to be the same, since the differences between the attenuated/non-attenuated are mutations in the surface protein (ectodomain). So, if one were only to replace the region encoding the cp45 HN ectodomain, the encoded protein would have the changes in the ectodomain from the cp45 HN, but the rest of the protein would be from the background virus.

In the same way, if Belshe were to replace the entire HN gene, the only differences between the original glycoprotein and the replacement heterologous protein would be in the

regions encoding the ectodomains. Therefore, the result of the two different methods of making is entirely expected to result in the same product, since the non-ectodomain regions of the background genome and the heterologous genome are the same. Methods of making do not lend patentability to the resulting products unless there is a structural and functional difference between a product made by one method versus the other. In this case, whether one replaces the entire gene or just the portion that encodes the heterologous ectodomain, the result is the same: a protein (whether it is called "chimeric" or not) comprising the cp45 HN mutations. The remainder of the non-ectodomain protein is the same (both structurally and functionally) as the background virus' protein. Therefore, the claims remain rejected for reasons of record.

Double Patenting

5. The provisional rejection of claims 1-30 and 46-74 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 144-215 of copending Application No. 09/083,793, is maintained for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. The provisional rejection of claims 1-30 and 46-74 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 53-85 of copending Application No. 09/458,813, is maintained for reasons of record. Although the conflicting

claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

7. The provisional rejection of claims 1-30 and 46-74 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 85, 88-92, 94-96, 98, 99, 101, 104, 107, 108, 113-117, 119, 122-126, 128-130, 132, 133, 135, 140, 141, 146-152, 154, 157, 159, 162 and 164 of copending Application No. 09/586,479, is maintained for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is encompasses the embodiments set forth in the instant claims. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. The provisional rejection of claims 1-30 and 46-74 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 180-222 of copending Application No. 09/733,692, is maintained for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the subject matter of the copending application is a species of the instantly claimed genus of PIVs, rendering the genus claims obvious. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

9. No claim is allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James C. Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Stacy B. Chen 4/17/06

Stacy B. Chen
Primary Examiner
April 17, 2006